L Number	Hits	Search Text	DB	Time stamp
2	47	Sodroski NEAR Joseph	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/06/08 17:24
3	80	Haseltine NEAR William	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/06/08 17:24
4	67	KINGSMAN NEAR ALAN	USPAT; US-PGPUB; EPO; JPO; DERWENT; USOCR	2004/06/08 17:24
15	40228	lentiviral lentivirus HIV$2	USPAT; US-PGPUB; EPO; JPO	2004/06/08 17:25
16	614	(lentiviral lentivirus HIV$2) and ((EF1$3 NEAR promoter) (PGK NEAR promoter))	USPAT; US-PGPUB; EPO; JPO	2004/06/08 17:25
1	28	Trono NEAR didier	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/06/08 17:25
5	1	LISZIEWCZ NEAR JULIANNA	USPAT; US-PGPUB; EPO; JPO; DERWENT; USOCR	2004/06/08 17:25
6	185	retrovir$15 and (HIV WITH U3)	USPAT; US-PGPUB; EPO; JPO; DERWENT; USOCR	2004/06/08 17:25
7	13	Naldini NEAR Luigi	USPAT; US-PGPUB; EPO; JPO; DERWENT; USOCR	2004/06/08 17:25
8	110	retrovir$15 and (HIV WITH U3 WITH R)	USPAT; US-PGPUB; EPO; JPO; DERWENT; USOCR	2004/06/08 17:25
9	183	Baltimore NEAR David	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/06/08 17:25
10	20	(Trono NEAR didier) and (lentivial HIV)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/06/08 17:25
11	37	verma NEAR inder	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/06/08 17:25
12	53	(lentivir$5 HIV) SAME (PGK EF-1)	USPAT; US-PGPUB; EPO; JPO; DERWENT; USOCR	2004/06/08 17:25
13	4	(("6136597") or ("5994136")).PN.	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/06/08 17:25

14	20	US-5686279-$.DID. OR US-5994136-$.DID. OR US-6013516-$.DID. OR US-6017758-$.DID. OR US-6084063-$.DID. OR US-6136597-$.DID. OR US-6165782-$.DID. OR US-6207455-$.DID. OR US-6218181-$.DID. OR US-6218186-$.DID. OR US-6242258-$.DID. OR US-6271359-$.DID. OR US-6277633-$.DID. OR US-6013516-$.DID. OR US-6096538-$.DID. OR US-6168916-$.DID. OR US-6235522-$.DID. OR US-6312682-$.DID. OR US-6312683-$.DID. OR US-6428953-$.DID. OR US-6440730-$.DID.	USPAT; US-PGPUB; EPO; JPO	2004/06/08 17:25
17	20	(lentiviral lentivirus HIV$2) and ((EF1$3 NEAR promoter)(PGK NEAR promoter)).clm.	USPAT; US-PGPUB; EPO; JPO	2004/06/08 17:25
18	58	((lentiviral lentivirus HIV$2) and ((EF1$3 NEAR promoter) (PGK NEAR promoter))) AND (posttranscriptional OR post NEAR transcriptional)	USPAT; US-PGPUB; EPO; JPO	2004/06/08 17:25
19	33	(US-6168916-$ or US-6235522-$ or US-6312682-$ or US-6096538-$ or US-6218187-$ or US-6051427-$ or US-5834256-$ or US-5858740-$ or US-5380830-$ or US-5981276-$ or US-6025124-$ or US-5665577-$ or US-6136597-$ or US-5994136-$ or US-6207455-$ or US-6165782-$ or US-5693508-$ or US-6132731-$ or US-6140114-$ or US-6576463-$).did. or (US-20030082789-$ or US-20030138954-$ or US-20030022303-$ or US-20030008374-$).did. or (WO-9712622-$ or WO-9931251-$ or GB-2331522-$ or WO-9817815-$ or WO-9817816-$ or WO-9817817-$ or WO-9727310-$ or WO-9631602-$ or WO-9637623-$).did.	USPAT; US-PGPUB; EPO	2004/06/08 17:25

> d his

(FILE 'HOME' ENTERED AT 18:28:53 ON 08 JUN 2004)

FILE 'MEDLINE, SCISEARCH, CAPLUS' ENTERED AT 18:29:14 ON 08 JUN 2004

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L1        475474 S LENTIVIR? OR HIV? OR RETROVIR?
L2           330 S EF1-ALPHA OR ELOGATION(L)FACTOR
L3            57 S L1 (L) L2
L4            36 DUP REM L3 (21 DUPLICATES REMOVED)
L5            13 S L4 AND PY<=2000
L6            13 SORT L5 PY
L7          2666 S MULTIPLE DRUG RESISTANCE
L8           186 S MULTIPLE DRUG RESISTANCE GENE
L9           238 S WOODCHUCK(L)REGULATORY OR WPRE
L10            0 S L1 (L) L2 (L) L8 (L) L9
L11            7 S L1 (L) L2 (L) L9
L12            3 DUP REM L11 (4 DUPLICATES REMOVED)
L13            0 S L1 (L) L2 (L) L8
L14           17 S L1 (L) L8
L15           12 DUP REM L14 (5 DUPLICATES REMOVED)
L16           12 SORT L15 PY
```

=> d an ti so au ab l12 1-3

L12 ANSWER 1 OF 3 MEDLINE on STN DUPLICATE 1
AN 2002325167 MEDLINE
TI Enhanced inhibition of human immunodeficiency virus type 1 replication by novel lentiviral vectors expressing human immunodeficiency virus type 1 envelope antisense RNA.
SO Human gene therapy, (2002 Jun 10) 13 (9) 1027-37.
Journal code: 9008950. ISSN: 1043-0342.
AU Mautino Mario R; Morgan Richard A
AB We have developed optimized versions of a conditionally replicating human immunodeficiency virus type 1 (**HIV**-1)-based **lentiviral** vector for gene therapy of **HIV**-1 infection. These vectors target **HIV**-1 RNAs containing sequences of the envelope gene by expressing a 1-kb fragment of the **HIV**-1 Tat/Rev intron in the antisense orientation. Expression of the envelope antisense gene (envAS) was evaluated under the control of different internal promoters such as the human phosphoglycerate kinase (PGK) promoter, the human **EF1-alpha** promoter, and the U3 region of the SL3 murine leukemia virus. The U3-SL3 promoter transactivates transcription from the vector **HIV**-1 LTR and drives higher expression levels of envAS-containing RNAs than other promoters in T-cell lines. The effect of other vector structural features was also evaluated. We found that the central polypurine tract and central termination sequence (cPPT) produce a small increase in vector infectivity of 2-fold to 3-fold and results in a 10-fold higher inhibition of wild-type viral replication in challenge experiments. The **woodchuck** hepatitis posttranscriptional **regulatory** element (**WPRE**) does not increase the cytoplasmic levels of envAS mRNA in T-cell lines. We observed that SupT1 and primary CD4(+) T cells transduced with these vectors showed high inhibition of **HIV**-1 replication, suppression of syncitium formation, and increased cell viability when infected with several **HIV**-1 laboratory strains. Our results suggest that higher vector copy number and increased levels of envAS RNA expression contribute to block replication of divergent strains of **HIV**-1.

L12 ANSWER 2 OF 3 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN DUPLICATE 2
AN 2000:861693 SCISEARCH
TI High-level transgene expression in human hematopoietic progenitors and differentiated blood lineages after transduction with improved lentiviral vectors
SO BLOOD, (15 NOV 2000) Vol. 96, No. 10, pp. 3392-3398.
Publisher: AMER SOC HEMATOLOGY, 1900 M STREET. NW SUITE 200, WASHINGTON, DC 20036.
ISSN: 0006-4971.
AU Salmon P; Kindler V; Ducrey O; Chapuis B; Zubler R H; Trono D (Reprint)
AB Recent experiments point to the great value of **lentiviral**

vectors for the transduction of human hematopoietic stem cells (hHSCs). Vectors used so far, however, have been poorly satisfying in terms of either biosafety or efficiency of transgene expression. Herein is described the results obtained with human immunodeficiency virus-based vectors optimized in both of these aspects. It is thus shown that vectors containing the **EF1 alpha** and, to a lesser extent, the phosphoglycerate kinase (PGK) promoter, govern high-level gene expression in human hematopoietic progenitors as well as derived hematopoietic lineages of therapeutic relevance, such as erythrocytes, granulocytes, monocytes, dendritic cells, and megakaryocytes. **EF1 alpha** promoter-containing **lentiviral** vectors can also induce strong transgene expression in primary T lymphocytes isolated from peripheral blood. A self-inactivating design: did net affect the performance of **EF1 alpha** promoter-based vectors but significantly reduced expression from the PGK promoter. This negative effect could nevertheless be largely rescued by inserting the post-transcriptional **regulatory** element of **woodchuck** hepatitis virus upstream of the vector 3' long terminal repeat. These results have important practical implications for the genetic treatment of lymphohematologic disorders as well as for the study of hematopoiesis via the lentivector-mediated modification of hHSCs. (C) 2000 by The American Society of Hematology.

L12 ANSWER 3 OF 3 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN DUPLICATE 3
AN 2000:889934 SCISEARCH
TI Lentiviral vectors for enhanced gene expression in human hematopoietic cells
SO MOLECULAR THERAPY, (NOV 2000) Vol. 2, No. 5, pp. 458-469.
Publisher: ACADEMIC PRESS INC, 525 B ST, STE 1900, SAN DIEGO, CA 92101-4495.
ISSN: 1525-0016.
AU Ramezani A; Hawley T S; Hawley R G (Reprint)
AB Accumulated data indicate that current generation **lentiviral** vectors, which generally utilize an internal human cytomegalovirus (CMV) immediate early region enhancer-promoter to transcribe the gene of interest, are not yet optimized for efficient expression in human hematopoietic stem/progenitor cells (HSPCs). As a first step toward this goal, we constructed self-inactivating derivatives of the **HIV** -1-based transfer vector pHR' containing the enhanced green fluorescent protein (GFP) gene as reporter and the **Woodchuck** hepatitis virus posttranscriptional **regulatory** element (**WPRE**). GFP expression was driven by a variety of strong viral and cellular promoters, including the murine stem cell virus (MSCV) long terminal repeat (LTR), a Gibbon ape leukemia virus (GALV) LTR, the human elongation factor 1 alpha (**EF1 alpha**) promoter, the composite CAG promoter (consisting of the CMV immediate early enhancer and the chicken beta -actin promoter), and the human phosphoglycerate kinase 1 (PGK) promoter. In contrast to results obtained in human embryonic kidney 293T cells and fibrosarcoma HT1080 cells, in which the CMV promoter expressed GFP at the highest levels, significantly higher levels of GFP expression (3- to 5-fold) were achieved with the MSCV LTR, the **EF1 alpha** promoter, and the CAG promoter in the human HSPC line KG1 alpha. Removal of the **WPRE** indicated that it stimulated GFP expression from all of the vectors in KG1 alpha cells (up to 3-fold), although it only marginally improved the performance of the intron-containing **EF1 alpha** and CAG promoters (<1.5-fold stimulation). The vectors using the MSCV LTR, the GALV LTR, and the PGK promoter were the most efficient at transducing primary human CD34(+) cord blood progenitors under the conditions employed. High-level GFP expression in the NOD/SCID xenograft model was demonstrated with the pHR' derivative bearing the MSCV LTR. These new **lentiviral** vector backbones provide a basis for the rational design of improved delivery vehicles for human HSPC gene transfer applications.

L16 ANSWER 4 OF 12 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1994:402596 CAPLUS
DN 121:2596
TI **Retroviral** mediated transfer of human **multiple drug resistance gene**
SO PCT Int. Appl., 89 pp.
CODEN: PIXXD2
IN Bank, Arthur; Goff, Stephen P.; Ward, Maureen
AB A mammalian retroviral producer cell constructed by transfecting a retroviral packaging cell with a retroviral vector containing the human multiple drug resistance (MDR) gene is provided. The mammalian retroviral producer cell produces retroviral particles suitable for transducing target cells. The producer cell of can be used to transduce target mammalian cell with the human MDR gene, and with a second, non-selectable gene, e.g., insulin, β-globin, or a major histocompatibility gene. The producer cell can be used in methods of treating a mammal afflicted with a cancer or a disorder characterized by abnormal expression of a non-selectable gene which involve transducing suitable cells from the mammal with the human MDR gene and the selecting with an MDR-responsive drug for cells which express the MDR gene. This producer line is demonstrated to be safe and free of replication-competent retrovirus. Transfer and expression of the human MDR gene in mice using a Harvey-based retroviral vector pHaMDR/A carrying human MDR cDNA were demonstrated.

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9409120	A1	19940428	WO 1993-US9988	19931015
	W: AU, CA, JP, US				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	CA 2146929	AA	19940428	CA 1993-2146929	19931015
	AU 9454445	A1	19940509	AU 1994-54445	19931015
	AU 687765	B2	19980305		
	EP 672119	A1	19950920	EP 1993-924952	19931015
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	JP 08506719	T2	19960723	JP 1993-510348	19931015

L6 ANSWER 12 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2000:383756 CAPLUS
DN 133:27363
TI Pseudotyping retroviral vectors by replacing the envelope glycoprotein with the lymphocytic choriomeningitis virus glycoprotein to increase host cell range
SO Eur. Pat. Appl., 69 pp.
CODEN: EPXXDW
IN Von Laer, Meike-dorothee
AB **Retroviruses** are pseudotyped by replacing the envelope glycoprotein with the gp glycoprotein of lymphocytic choriomeningitis virus. This pseudotyping increases the range of cells that the nucleic acids can be delivered to. Packaging cells have the env gene deleted and the gp gene under control of a strong promoter, e.g. from cytomegalovirus or the **EF1.alpha.** gene. Packaging still requires functional **retroviral** gag and pol genes. Use of the protein to pseudotype murine leukemia virus and human immunodeficiency virus is demonstrated.

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 1006196	A2	20000607	EP 1999-250415	19991125 <--
	EP 1006196	A3	20000621		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	DE 19856463	A1	20000608	DE 1998-19856463	19981126 <--
	US 6589763	B1	20030708	US 2000-718096	20001122

upstream of the vector 3' long terminal repeat. These results have important practical implications for the genetic treatment of lymphohematologic disorders as well as for the study of hematopoiesis via the lentivector-mediated modification of hHSCs. (C) 2000 by The American Society of Hematology.

L6 ANSWER 8 OF 13 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
AN 2000:588618 SCISEARCH
TI Therapeutic levels of human factor VIII and IX using HIV-1-based lentiviral vectors in mouse liver
SO BLOOD, (**1 AUG 2000**) Vol. 96, No. 3, pp. 1173-1176.
Publisher: AMER SOC HEMATOLOGY, 1900 M STREET. NW SUITE 200, WASHINGTON, DC 20036.
ISSN: 0006-4971.
AU Park F; Ohashi K; Kay M A (Reprint)
AB **Lentiviral** Vectors have the potential to play an important role In hemophilia gene therapy. The present study used human immunodeficiency virus (**HIV**)-based **lentiviral** vectors containing an **EF1 alpha** enhancer/promoter driving human factors VIII (hFVIII) or IX (hFIX) complementary DNA expression for portal vein injection Into C57B1/6 mice. Increasing doses of hFIX-expressing **lentivirus** resulted in a dose-dependent, sustained increase in serum hFIX levels up to approximately 50-60 ng/ml, Partial hepatectomy resulted in a 4- to 6-fold increase ($P < 0.005$) in serum hFIX of up to 350 ng/mL compared with the nonhepatectomized counterparts. The expression of plasma hFVIII reached 30 ng/mL (15% of normal) but was transient as the plasma levels fell concomitant with the formation of anti-hFVIII antibodies, However, hFVIII levels were persistent in immunodeficient C57BI/6 scid mice, suggesting humoral immunity-limited gene expression in immunocompetent mice. This study demonstrates that **lentiviral** vectors can produce therapeutic levels of coagulation factors in vivo, which can be enhanced with hepatocellular proliferation. (C) 2000 by The American Society of Hematology.